Radioisotope Production for Nuclear Medicine

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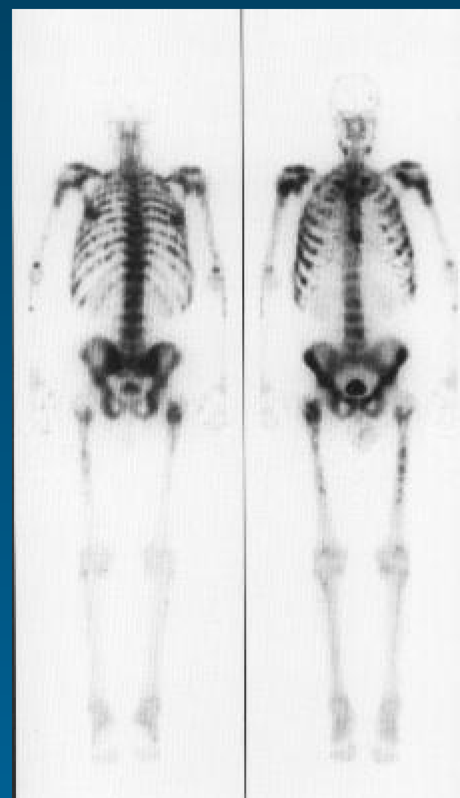
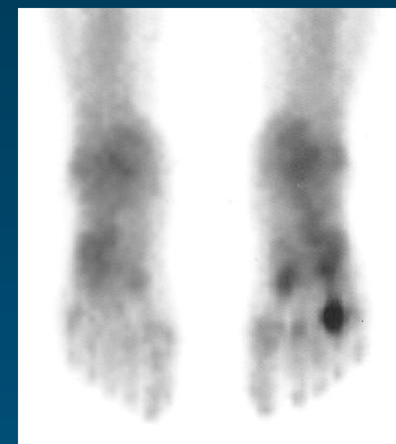
- Radioisotopes are crucial to modern patient care
- 15 million nuclear medicine procedures per year in the US for diagnosis or therapy

MDP imaging, Met's and Fracture





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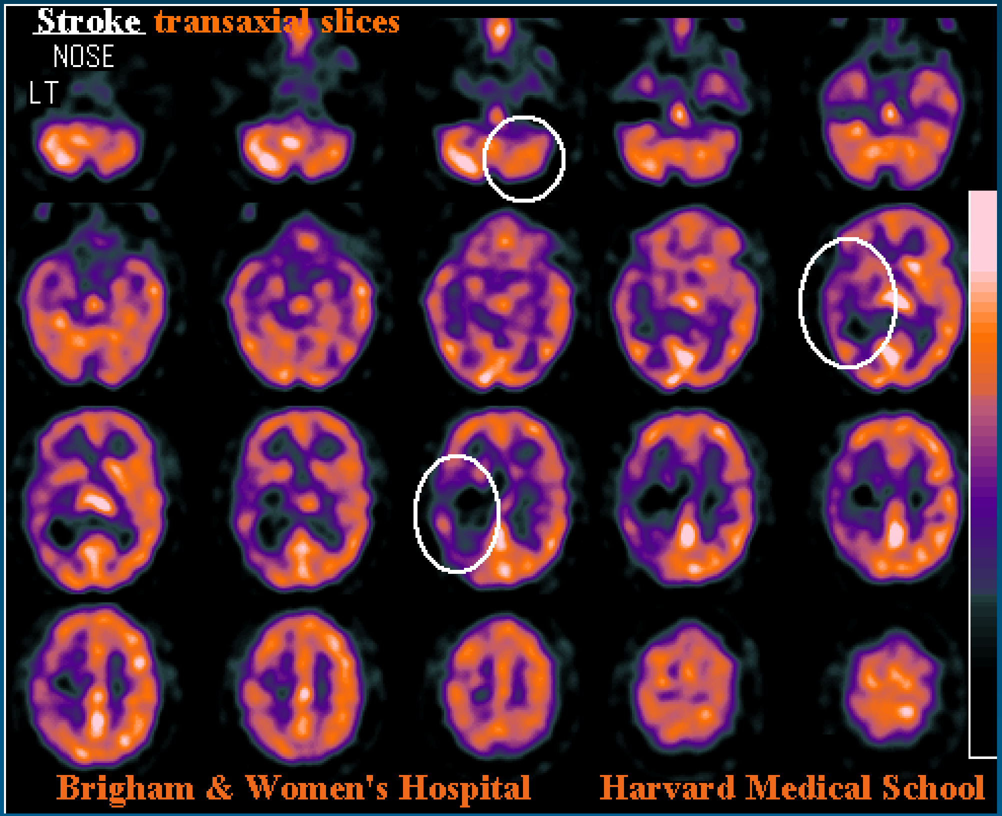

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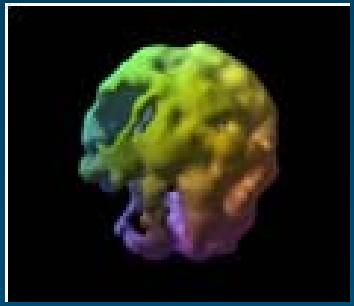

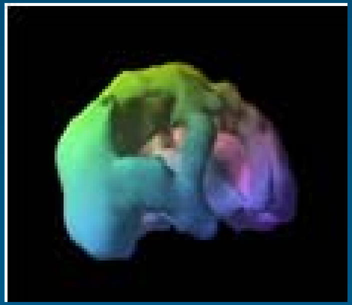

http://www.brainplace.com/bp/atlas/default.asp

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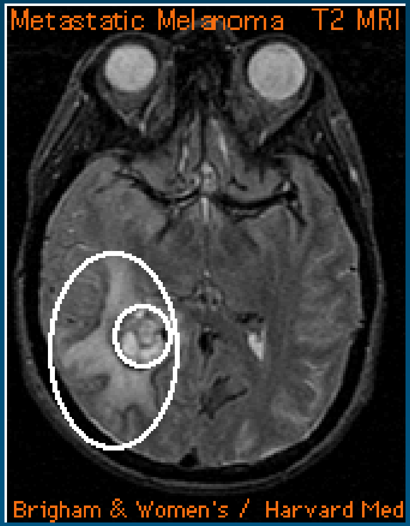
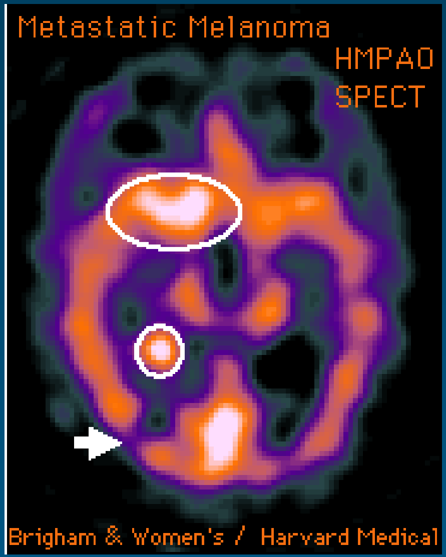
Metastatic Melanoma





http://brighamrad.harvard.edu/education/online/BrainSPECT/BrSPECT.html

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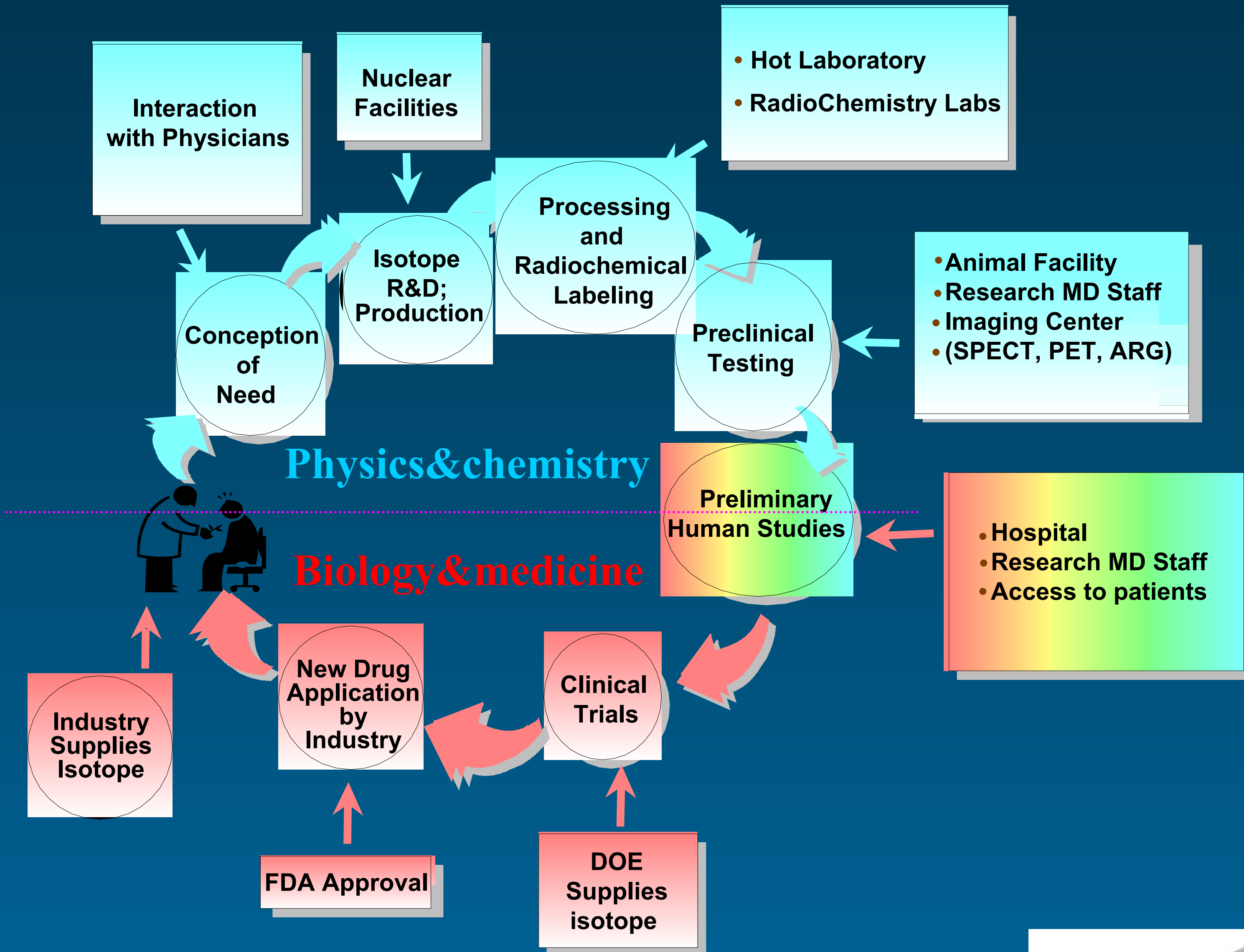
Interdisciplinary nature of Nuclear Medicine



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Definitions

- **Radioisotope:** unstable form of an element that spontaneously "decays" with the emission of energy
- **Half life:** the time required for an initial large number of nuclei to be reduced to half that number by decay
- Decay rate given by

$$N=N_0\exp[-\ln 2(t/t_{1/2})]$$

- **Radiopharmaceutical:** a carrier molecule containing a radioisotope, administered in trace quantity, designed to target a specific organ or physiological function

Properties of Radioactive Emissions

- **alpha particles** are helium nuclei (2 protons & 2 neutrons); non penetrating (stopped by one sheet of paper or skin); very toxic to cells; potential use for cancer therapy
- **beta particles** are energetic electrons or positrons (antielectrons); low penetration; toxic to cells; used in cancer therapy
- **gamma rays** are high energy electromagnetic radiation; highly penetrating; less toxic to cells; critical to diagnostic imaging
- **Auger electrons** are low energy atomic electrons; non penetrating; very toxic to cells; potential use for cancer therapy

Units of radioactivity

- Becquerel (Bq) is one disintegration per second;
- Curie is an older but still common unit which is the disintegration rate from 1 gram of radium-226 and is equivalent to 3.7×10^{10} disintegrations per second; this is a lot so millicurie (mCi) and microcurie (µCi) are also commonly used.
- Rad is energy absorbed (dose) and is 100ergs per gram, but the newer unit is the Gray (Gy)=100rad
- Roentgen (R) is the unit of radiation exposure that produces in air 1 esu of electricity. Absorbed in water 1R is ~0.93 rad
- Roentgen equivalent man (Rem) is the product of the exposure in R and a biological weighting factor. 1Rem=1.0785R . Average annual background dose in the US is 300mRem. The newer unit is the Sievert=100Rem.

Sources of Radioisotopes

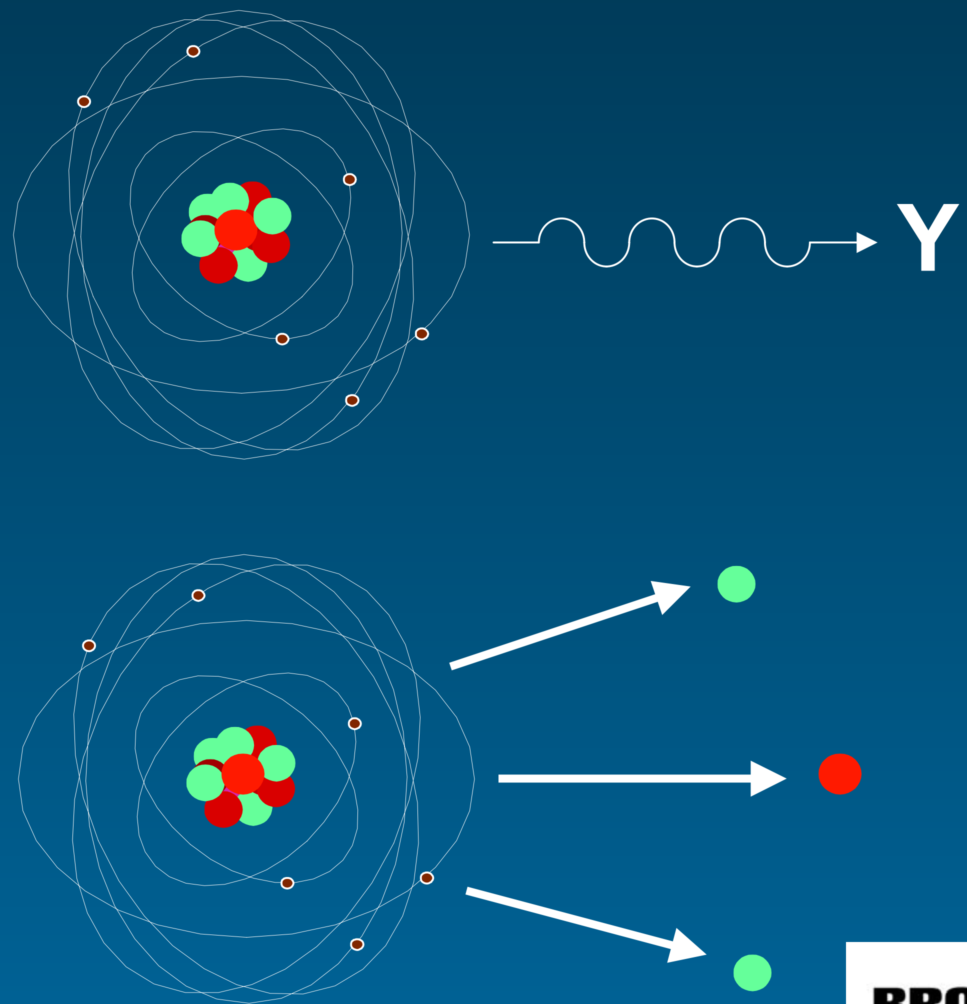
- Naturally Occurring
  - primordial (eg. Uranium-238, Potassium-40)
  - produced continuously in the atmosphere by cosmic rays (eg. Carbon-14, tritium, Beryllium-7) and fall to earth
- Man made
  - reactor produced with neutrons
  - accelerator produced with protons or other charged particles

Projectile/Target Processes

- Electron excitation and ionization
- Nuclear elastic scattering
- Nuclear inelastic scattering with or without nucleon emission
- Projectile absorption with or without nucleon emission
- If the product nucleus is different from the target nucleus a nuclear reaction occurred

Major Nuclear Reaction Types

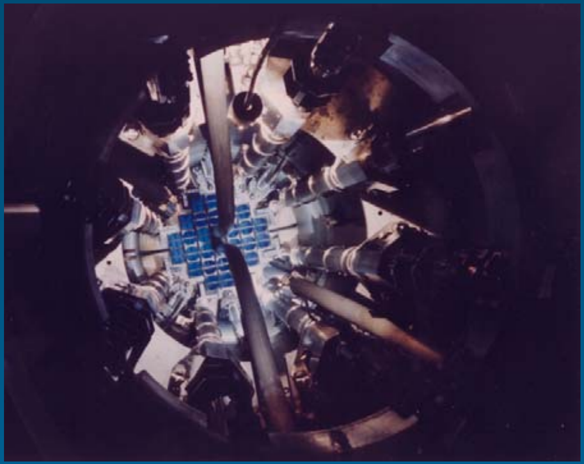
Target Nucleus



Radioisotope Production Reactor

The experimental area of a research reactor

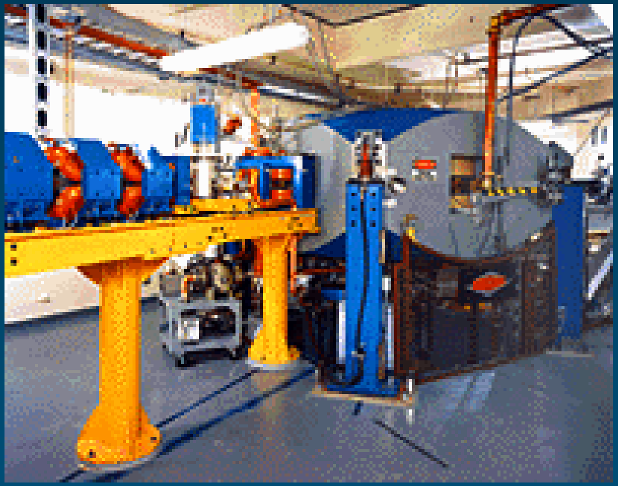
Core of the reactor showing tubes for insertion/retrieval of isotope targets



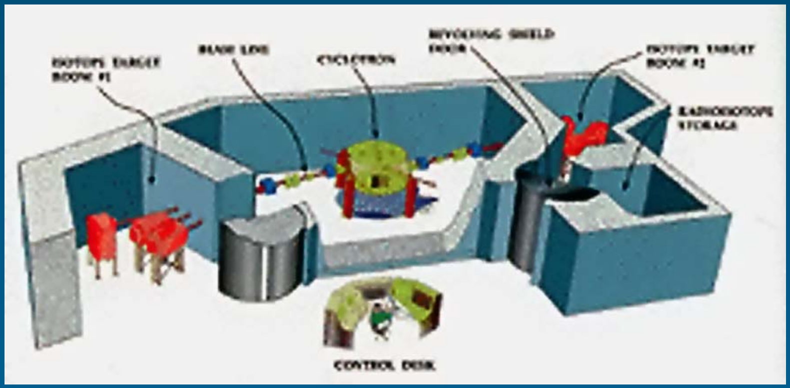

RHIC
BOOSTER
LINAC
AGS
BLIP
HTB
TANDEM
HITL

Accelerators for Isotope Production-Cyclotron

A commercial low energy isotope production cyclotron; in the U.S. approximately 24 are operated by industry and 100 by medical centers



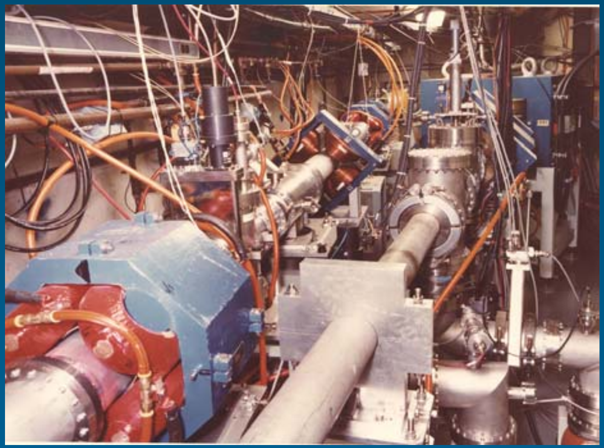
Typical facility layout for purchased system



Accelerators for Isotope Production-LINAC

The high energy proton LINAC at Brookhaven National Laboratory

Beam lines to direct protons to production targets (BLIP)



The Radioisotope Generator

- If a long lived “parent” radioisotope decays into a short lived “daughter” radioisotope and if the parent and daughter are chemically separable

- Then a “generator” or cow is a practical, convenient method to transport and use (milk) very short lived radioisotopes without having to produce them at each site

- This technique has been of utmost importance to nuclear medicine, especially the $^{99}Mo/^{99m}Tc$ system (66h/6h)

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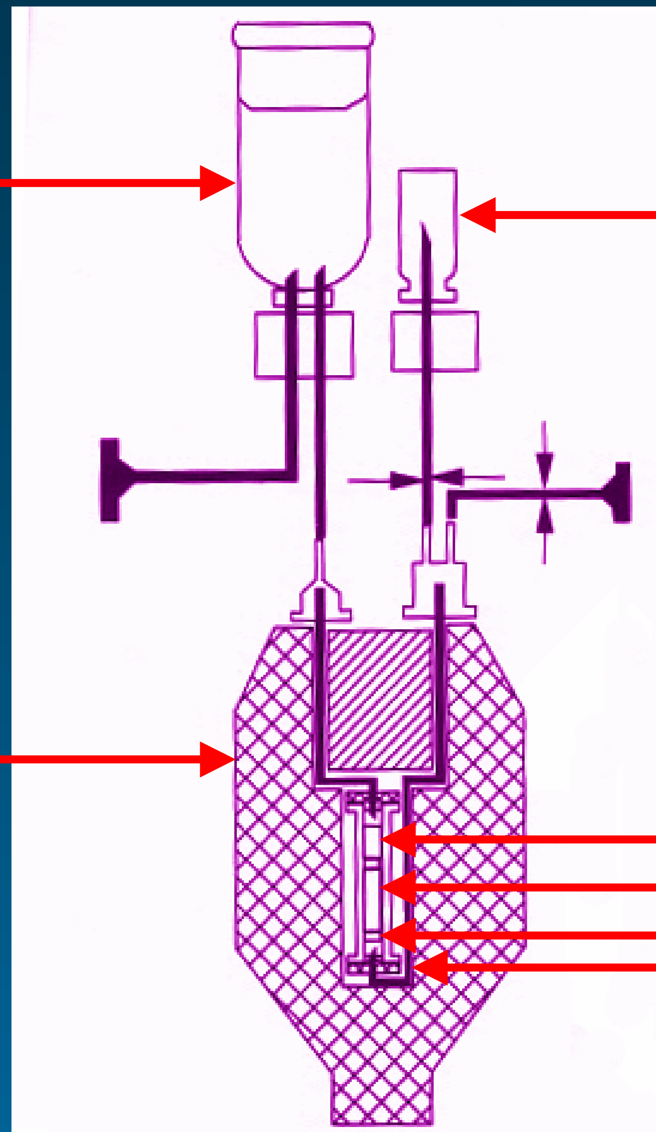
Schematic Diagram of Molybdenum-99/ Technetium-99m Generator



Radioisotope Processing and Purification

- All isotope production targets require some chemical processing
- Radiation shielding for the chemist is often required, so “hot cells” are often used

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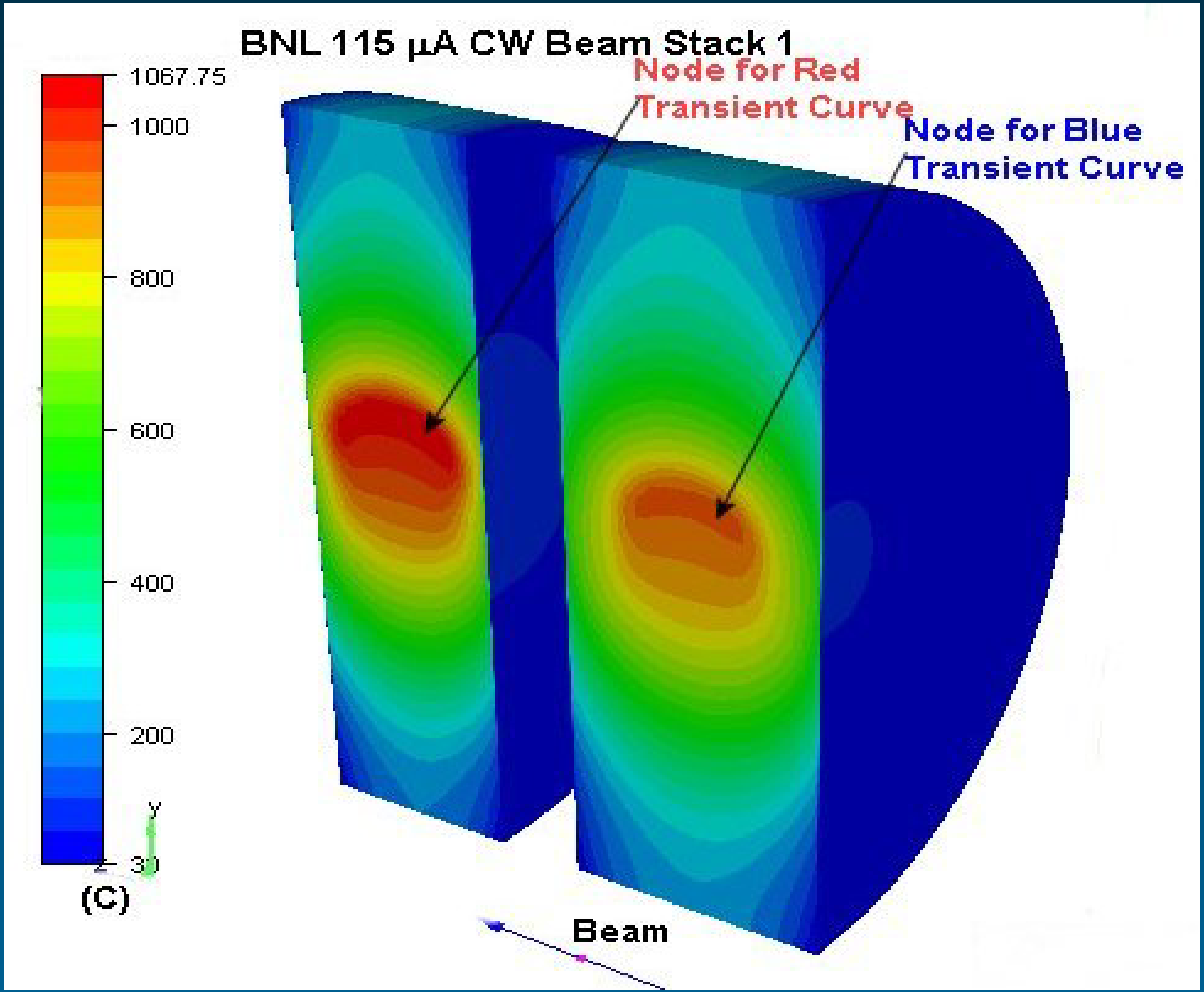
Target Characteristics

- Particle beams carry a lot of energy and heat targets (30kW at BLIP)
- Physical factors:
  - isotopic abundance; vapor pressure; crystal form and pressibility; thermal properties; melting & boiling point; thermal conductivity
- Chemical factors:
  - thermal stability against decomposition; corrosiveness; convenient inorganic compounds; available in high purity


BNL 115 µA CW Beam Stack 1
Node for Red Transient Curve
Node for Blue Transient Curve
1067.75
1000
800
600
400
200
30
(C)
y
Beam

Chemical Processing Methods

- Solvent extraction involves selective partitioning between two immiscible solvent phases
- Ion exchange chromatography involves differences in distribution of a complex between a mobile phase and a stationary phase (typically a resin packed in a column)
- Distillation exploits differences in volatility between target and product
- Precipitation is less important in nuclear medicine applications. With high specific activity there is not enough mass to collect a precipitate and handling precipitates remotely can be difficult

Some Common Clinically Used Isotopes

Isotope	Half life	Facility	Medical Applications
Molybdenum-99/ Technetium-99m	2.75d/ 6.0h	reactor*	numerous diagnostic scans
Thallium-201	73h	cyclotron**	heart stress test
Iodine-131	8.0d	reactor*	thyroid function & Rx, cancer Rx
Iodine-125	60.1d	reactor*	prostate cancer Rx, research
Xenon-133	5.3d	reactor*	lung function
Indium-111	2.8d	cyclotron**	inflammation & tumor detection
Gallium-67	3.2d	cyclotron**	inflammation & tumor detection
Strontium-89	14.3d	reactor*	bone cancer Rx
Palladium-103	17.0d	cyclotron**	prostate cancer Rx
Fluorine-18	110m	cyclotron**†	cancer detection & brain research
Yttrium-90	2.7d	reactor waste	cancer Rx

*foreign; **domestic industry; †domestic hospital & university

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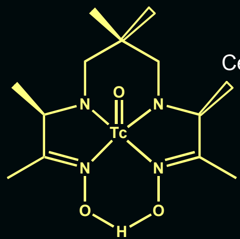
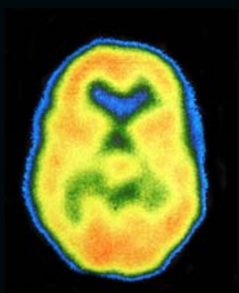
Technetium-99m

Ceretec®



Brain Imaging



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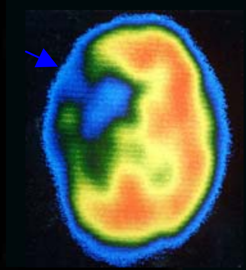

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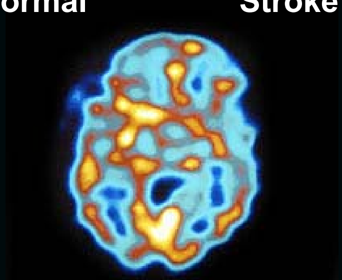
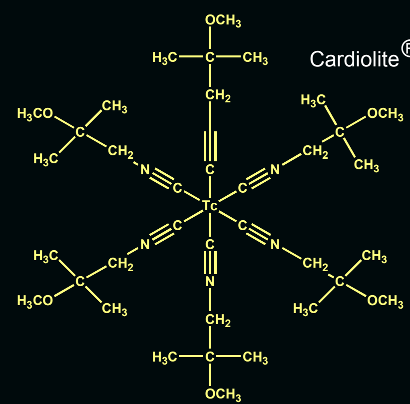


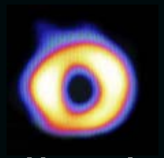
Epilepsy

Cardiolite®



Heart Imaging

Normal



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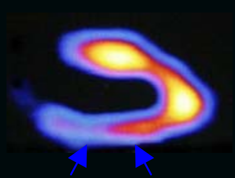
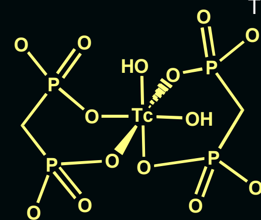


Heart Attack

Technescan-MDP®



Bone Imaging

Normal

Metastatic
Prostate Cancer

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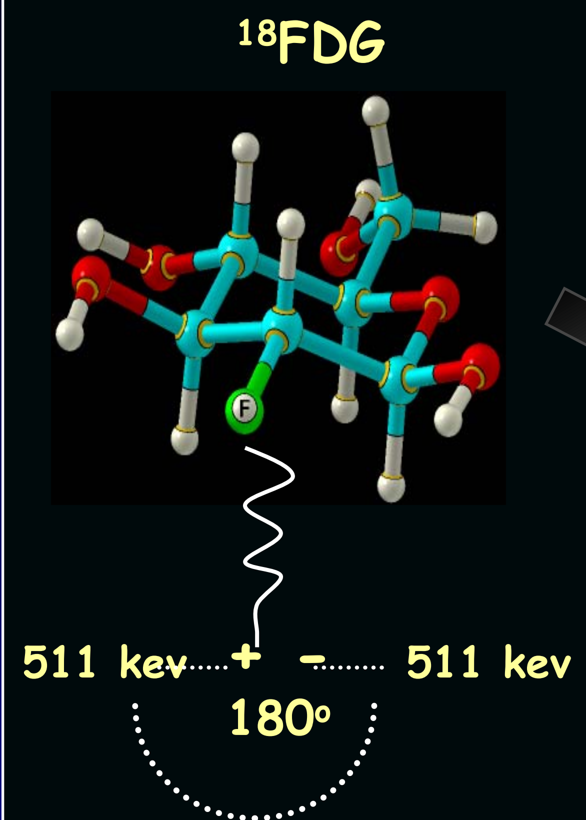
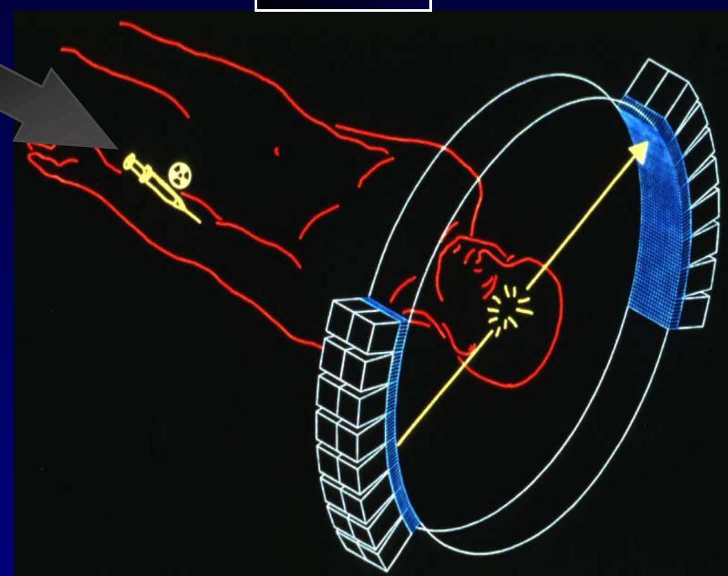
Positron Emission Tomography (PET)



Radiotracer



PET Scanner

PET Image

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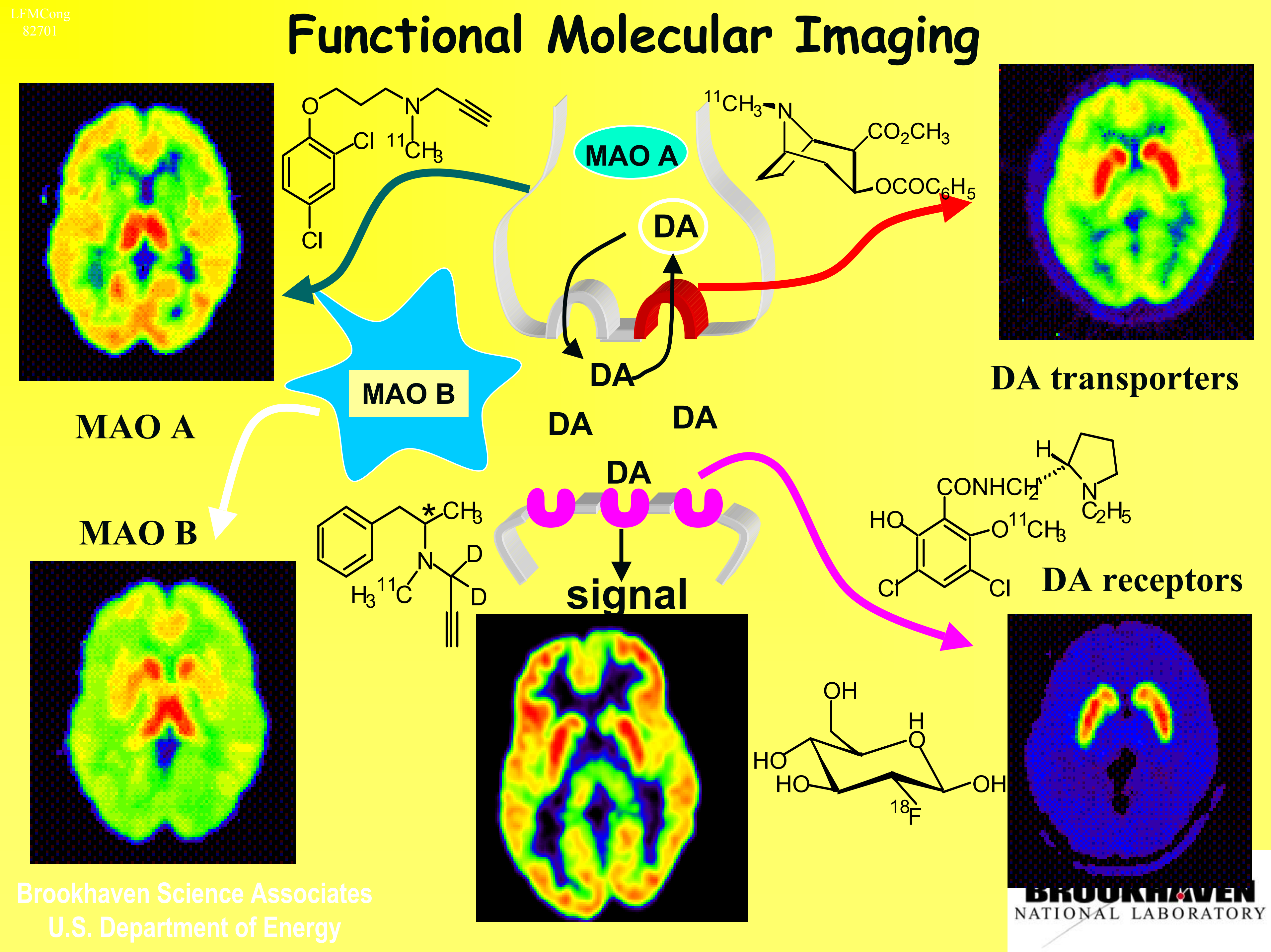
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Functional Molecular Imaging
MAO A
DA
MAO B
DA
DA
DA
DA
signal
MAO A
MAO B
DA transporters
DA receptors
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Po-210 – an isotope in the headlines

- Polonium-210 is an alpha emitting radioisotope with a physical half life of 138.4d and it occurs naturally all over the earth at low levels.
- It is produced by neutron irradiation of bismuth metal to form Bi-210 which beta decays with a 5.0d half life to Po-210. The Po-210 is chemically separated from the Bi target.
- It is used commercially in antistatic devices.
- It is hazardous only inside the body and has a biological half life of 50d, concentrating mostly in spleen and liver.
- About 1 microgram ingested can be lethal.
- It is not produced at BNL.